

In the specification:

Insert the paper copy of the Sequence Listing filed herewith following the Oath/Declaration.

Replace the paragraph beginning at page 5, line 15 with the following rewritten paragraph:

Ten segments in the gene encoding HBsAg, HBsAg1-10 (SEQ ID NOs: 1-10), were selected as targets for RNA interference. To generate vectors that encode iRNAs targeting these segments, oligonucleotides containing each of these sequences ("sense strand") and their inverted repeats ("anti-sense strand") were synthesized using a standard method. In each of the oligonucleotides, the sense and antisense strands ("N₁₉"), 19 nucleotides in length, are separated by a spacer of 9 nucleotides. The complements of these oligonucleotides were also synthesized and allowed to form double-stranded DNAs with these oligonucleotides, respectively. An exemplary double-stranded DNA is shown below.

5' - GATCCCCN₁₉ttcaagagaN₁₉TTTTTGAAA-3' (SEQ ID NO:11)
3' - GGGN₁₉aagttctctN₁₉AAAAACCTTTTCGA-5' (SEQ ID NO:12)

As shown above, each double-stranded DNA contained sequences flanking the N₁₉-spacer-N₁₉ segment (boxed), which created 5' overhangs of Bgl II and Hind III at its two ends (underlined) to facilitate subsequent cloning. The double-stranded DNA was then ligated into a pSUPER vector (Dr. Reuven Agami, Plesmanlaan 121, 1066 cx Amsterdam, Netherlands) that had been digested with Bgl II and Hind III. The resultant vectors, once introduced in mammalian cells, transcribed hairpin RNAs. The pHsU6-+1 vector (Dr. Wen-Tsen Chang, Department of Biochemistry, NCKU Medical College, Tainan Taiwan 70101, ROC) was also used to construct vectors to generate hairpin RNAs. Shown below is an exemplary double-stranded DNA for cloning into this vector. It had 5' overhangs of Cla I and Hind III.

5' - CGN₁₉ttcaagagaN₁₉CTTTTTTGAAA-3' (SEQ ID NO:13)
3' - N₁₉aagttctctN₁₉GAAAAACCTTTTCGA-5' (SEQ ID NO:14)

Replace the paragraph beginning at page 10, line 16 with the following rewritten paragraph:

The serum HBV-DNA level in the injected mice was also measured. Mouse sera were collected at day 2 after the injection. The sera were treated with DNaseI (20U, >12 hours) to eliminate plasmid DNA. HBV DNA was then purified from 200 µl mouse serum using a viral DNA/RNA isolation kit (Maxim Biotech, INC., San Francisco, CA). Five microliters of the isolated DNA was subjected to a PCR analysis. The primers SP2-d1 (5'-GCGGGTCACCATATTCTTGG-3' (SEQ ID NO:15)) and SP2-d4 (5'-GAGTCTAGACTCTGCGGTAT-3' (SEQ ID NO:16)) were used to amplify the preS2 region of the surface antigen gene. It was found that serum HBV-DNA was completely inhibited by pSUPER-HBsAg-3. These results indicate that the RNAs transcribed from the RNAi vector inhibit the replication of the whole HBV genome.